

ANALGESIC COMPOSITION

【Technical Field】

The present invention relates to an analgesic composition comprising extract of
5 Pulsatillae Radix as active ingredient. Specifically, the present invention relates to the
analgesic composition which alleviates pain of cancer patient and has low side effects.

More specifically, the present invention relates to the analgesic composition
comprising extract of Pulsatillae radix as active main ingredient and if necessary, more
comprising one or more extracts selected from the group consisting extract of Ginseng Radix,
10 extract of Glycyrrhizae Radix, extract of pericarp of Akebia quinata and extract of the bark of
Cortex Ulmi as auxiliary ingredient(s).

Various cancer cells which grow in cancer patients affect various influences to hosts.
Growing cancer induces hyperthermia, anorexia, loss of weight, microbiosis, anemia,
destruction of hormone balance, neurosis, pressure to marginal tissue or organ, occlusion of
15 intestinal tract or blood vessel, indifferent invasion, destruction of tissue, influence to ter-
tissue by metastasis, blood circulation of virulent material, etc., to induce of severe pain to
host to come to death.

Therefore, the pain of cancer patient is commonly very severe and difficult to be
controlled and clinically intensive toxic analgesic should be used. An example of pain by
20 destruction of tissue is ostalgia. The ostalgia is induced by an irritation which induced by
cancer cell which is irrputed or transferred into bone tissue or by fracture. A cancer patient is
very sensitive to microbiosis by loss of protective power of the patient, by destruction of
protective mechanism through cancer therapy and by retention of fluid through obstruction.

An example of obstruction of blood vessel by tumor occurred in limited tissue is brain tumor and pain is induced by pressing blood vessel and meninx because of occurrence of tumor in brain blood vessel.

Tumor growing in intestinal tract stretches and/or presses and/or obstructs the tract and induces pain. However, tumor gradually growing in the tract is sometimes already progressed before complaint of pain. For example, stomach cancer, pancreas cancer, rectal cancer and liver cancer, etc. often do not induce pain until considerable progress of the cancers. In another case, pain does not arise at the very site of the cancer but arise at another site. For example, in the case of cancer occurred in the intestinal tract, because irritation transfer enters through sympathetic nerve into spiral marrow, pain sometimes occurred a very distant area from the site of the cancer.

As for analgesic for the treatment of the pain of cancer or tumor, a very intensive analgesic is used sometimes together with auxiliary ingredient. The mostly used analgesic is morphine or derivative derived from morphine. As for such auxiliary material, calcium channel agonist and antagonist including N-methyl-D-aspartate(NMDA) antagonist and topical and general anesthetics are used.

However, analgesics used until now can not reduce 100% of pain of cancer patient and have drug tolerances and side effects. Therefore, In order to treat pain of cancer, it is ideal that an analgesic which has antitumor activity and less side effect and analgesic effect at the same time is developed.

【Background Art】

The development of analgesic based upon roots of plants (Pulsatillae Radix) of Pulsatillae species has merit that Pulsatillae Radix is a powerful anticancer material. In fact, in

case any cancer or tumor is treated, pain is naturally disappeared. According to experiences of the inventors, patients who were administered preparation of Pulsatillae Radix felt reductions of pains and even though cancers were not treated perfectly and became to death, during the state that patients were not treated with Pulsatillae preparation, the patients declared that pains
5 were reduced substantially.

Pulsatillae Radix is the root of Pulsatillae species which belong to Ranunculaceae plant. All the roots can be used in the present invention. In oriental medicine, Pulsatillae Radix is used for the purpose of treating child bed fever, detoxification, antidiarrhea, bactericide, amebicide, fungicide (Chinese medicine encyclopedia).

10 Recently, the Pulsatillae Radix is reported to have antitumor activity and is now under clinical trial. Prior arts are illustrated as follows:

1. Hsu et al.; Oriental Materia Medica pp 226-227, Oriental Healing Art Institute, 1986, CA, USA,

15 2. Korea Patent Nos. 72,982 and 312,622.

Panax Ginseng has various pharmaceutical activities such as anti-stress and anti-diabetes activities. Specifically, according to mouse writhing test, ginsenoside Rf among ginsenosides which Ginseng Radix has was reported to have analgesic activity(1). In addition,
20 though US Patent No. 5,417,979 teaches that a raw plant drug composition comprising Glycyrrhizae Radix as main component has analgesic activity, the said patent only teaches that the composition can be used as auxiliary. However, the selectivity of main plant drug, specialty of anticancer analgesic or preparation method thereof is different from the present invention.

1. Mogil JS, Shin YH, McCleskey EW, Kim SC, Na Sy, Brain Res 792, 218-228(1998).

2. US Patent No. 5,417,979.

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Glycyrrhizae Radix is used as tonic, neutralization, analgesic, detoxification, cough medicine or resolute in oriental medicine. Various studies for protection of liver, anticancer property etc. were carried out.

Pericarp of Akebia quinata is a fruit of Akebia quinata and is used as lumbago, intercostal neuralgia, gastralgia, urethra calculosis, menoxenia or diarrhea. The Pericarp of Akebia quinata has akebia saponin. But, no literatures that Pericarp of Akebia quinata is used as analgesic have published until now.

Ulmi cortex is a bark of Ulmus species or a bark of root of the Ulmus species and is used resolute in oriental medicine. Recently, a literature reports that extract of the Ulmi cortex prevents local or systemic anaphylaxis (1).

1. Kim HM, Shin HY, Choi IY, Lee EH, Lee EJ, Action of Ulmi radicle cortex extract on systemic and local anaphylaxis on rats. Gen. Pharmacol. 31, 483-488 (1998).

20 **【Disclosure of Invention】**

One object of the present invention is to provide an analgesic composition comprising an extract of Pulsatillae Radix as active ingredient.

The other object of the present invention is to provide an analgesic composition comprising an extract of Pulsatillae Radix as active ingredient and one or more ingredient(s)

selected from the group consisting extract of Ginseng Radix, extract of Glycyrrhizae, extract of Radix Pericarp of Akebia quinata and extract of Ulmi cortex as auxiliary ingredient(s).

It is not known until now which compound of Pulsatillae Radix has analgesic effect. In spite of that, in case any preparation comprising the Pulsatillae Radix has good anticancer effect, it is natural that pain reduces. Accordingly, the present inventors determined that it is important that raising of concentration of anticancer material of the Pulsatillae Radix is important.

Korean Patent Nos. 72,982 and 312,622 teach that solvent fractions were prepared from Pulsatillae Radix in order to prepare anticancer preparations. However, there were some uncertainties of establishment of formation conditions of anticancer materials and were used mainly first fractions of extracts. Hederagenin-3-O- α -L-rhamnopyranosyl(1 \rightarrow 2)-[β -D-glucopyranosyl(1 \rightarrow 4)]- α -L-arabinopyranoside(Code No. SB365) was isolated as anticancer material from the Pulsatillae Radix. The inventors tried to improve analgesic effect of the Pulsatillae Radix by preparing preparation in which SB365 is accumulated in high concentration.

The extracting procedures are as follows: To certain parts of powder of the Pulsatillae Radix is added a certain parts of solvent and the mixture is extracted at a certain temperature for various hour(s) and measures the contents of SB365. The extracting temperature is under 60 °C, desirably 20-50 °C, more desirably 25-35 °C. 2-10 parts of solvent, desirably 2-3 parts are used per 1 part of the Pulsatillae Radix. Maintaining paste state of the mixture is desirable method, for the sides of kinetics or easiness of work up method because chemical reaction is comparative to concentrations of substrates and catalysis (enzymes)

(under the condition that hydrolysis by hydrolase). Based upon the change with the passage of time, reaction time is most desirable at about 30 °C.

As for work up method after extraction, common evaporation of solvent, drying method or lyophilization can be used. Lyophilization is most desirable.

5 As for solvent for extracting plant substances, water, methanol, ethanol, propanol, butanol, methylenechloride, acetone or mixture thereof can be used. Water, methanol, ethanol or mixture thereof is more desirable. Water or 50 % (V/V) alcoholic solution is most desirable.

The composition of the present invention can be prepared in the form of solution,
10 injection, powder, tablet, capsule with vehicle commonly used in the pharmaceutical field.

【Brief Description of the Drawing】

Fig. 1 shows TLC of extract of Pulsatillae Radix (PKW).

15 【Best Mode for Carrying Out the Invention】

The present invention is explained in more detail with the examples and experiments below.

General examples

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General example 1

Preparation of basic extract from Pulsatillae Radix

1) 1 weight part of Pulsatillae Radix is mixed with 1 - 100 weight part(s) of water or lower alcohol solution of water of 50%(v/v) and the mixture is covered with gauze or filter

paper and with cover. The mixture is reacted at or under 60°C for about 30min and the mixture is filtered. Filtrate is stored and remaining residue is mixed with 2-10 weight parts of lower alcohol of 20-80 % (v/v). The mixture is stirred for about 15 min and filtered. The combined filtrate is evaporated under reduced pressure to obtain residue. To the residue is
5 added 2-10 weight parts of methanol or ethanol and the mixture is stand for about 10 min. Insolubles are filtered to obtain a solution. The solution is evaporated to obtain an extract of yellowish brown (PKW fraction).

Yield of the PKW fraction is 28-35 weight %. The PKW fraction can be used as anticancer agent or analgesic of the present invention or can be used as basic ingredient for
10 further composition. The PKW fraction has much SB365 contents than that which is extracted from any other solvent such as organic solvent, water-containing organic solvent.

2) The combined solution of 1) of the general example 1 is instantly lyophilized to obtain an extract of yellowish brown.

15 **General example 2**

Preparation of extract of Ginseng Radix (PKG)

1) 1 weight part of Ginseng Radix is mixed with 5 - 100 weight parts of water and extracted at room temperature for about 2hrs and the mixture is filtered. Filtrate is stored and remaining residue is mixed with alcoholic water of 20-80 % (v/v) and filtered. The combined
20 solution is evaporated to obtain an extract. The extract is titled to PKG.

2) The combined solution of 1) of the general example is instantly lyophilized to obtain an extract of Ginseng Radix.

General example 3

Preparation of extract of Glycyrrhizae Radix (PKly)

1) 1 weight part of powder of Glycyrrhizae Radix is mixed with 2-500 weight parts of water and extract at room temperature for 2hours, filtered and dried to obtain extract of Glycyrrhizae Radix (PKly).

5 2) The filtrate obtained from 1) is instantly lyophilized to obtain an extract of Glycyrrhizae Radix (PKly).

General example 4**Preparation of extract of Pericarp of Akebia quinata (PKake)**

10 1) 1 weight part of powder of Pericarp of Akebia quinata is mixed with 10-50 weight parts of alcoholic water of 20-50%(V/V) and extracted at room temperature for 2hours, filtered and evaporated under reduced pressure to obtain extract of Pericarp of Akebia quinata(PKake).

15 2) The filtrate obtained from 1) is lyophilized to obtain an extract of Pericarp of Akebia quinata(PKake).

General example 5**Preparation of extract of Ulmi cortex (PKu)**

20 1) 1 weight part of powder of Glycyrrhizae Radix is mixed with 5-50 weight parts of water or alcoholic ethanon of 20-80%(V/V) and extracted at room temperature for 2hours, filtered and dried to obtain extract of extract of Ulmi cortex(PKu).

2) The filtrate obtained from 1) is instantly lyophilized to obtain an extract of Ulmi cortex (PKu).

Examples

Example 1

Preparation of extract from Pulsatillae Radix(PKW)

- 5 1) In a beaker of 100ml, there added 30g of powder of Pulsatillae Radix and 60ml of water and is mixed to obtain a paste. The paste is covered with gauze which is wetted with water and the paste is stand at 30 °C for 1hour. The paste is added to a beaker of 300ml and 240ml of methanol is added thereto and stirred with magnetic stirrer. After stirring, the mixture is filtered and the remaining on the filter is added to the beaker and 300ml of
- 10 alcoholic water of 50% (V/V) is added thereto and the mixture is stirred for 20min., filtered. The combined filtrate evaporated under reduced pressure to dryness. To the dried residue there added 200ml of methanol, stirred, stood for 1hour and filtered. The obtained filtrate is dried to obtain 11.3g of pale yellow residue which is titled to PKW of which TLC is shown to Fig. 1. In the Fig. 1, left is developed with methanol solution (PKE), center is developed with
- 15 Methanol insoluble material and right is developed with SB 365.

2) The last filtrate is immediately lyophilized to obtain the same contents of extract of which TLC is the same with that of Fig.1.

Example 2

20 Preparation of extract of Ginseng Radix (PKG)

1) 15g of powder of dried fine roots of Ginseng Radix is mixed with 100ml of water and the mixture is stirred at room temperature for about 1hr and filtered. To the filter cake there added 100ml of ethanolic water of 50% (V/V), stirred for 1 hr and filtered. The combined filtrate is evaporated to obtain 5.4g of brown tar (PKG).

2) The combined solution of 1) of the example 2 is instantly lyophilized to obtain the same amount of extract of Ginseng Radix.

Example 3

5 Preparation of extract of Glycyrrhizae Radix (PKly)

1) 4.5g of powder of Glycyrrhizae Radix is dispersed with 50ml of water and extract at room temperature for 1hour, filtered and dried to obtain 1.9g of extract of Glycyrrhizae Radix (PKly).

2) The filtrate obtained from 1) is instantly lyophilized to obtain the same amount of
10 extract of Glycyrrhizae Radix (PKly).

Example 4

Preparation of extract of Pericarp of Akebia quinata (PKake)

1) 10g of powder of Pericarp of Akebia quinata is mixed with 100ml of alcoholic
15 water of 50%(V/V) and extract at room temperature for 2hours and filtered. The residue is extracted with the same way and filtered. The combined filtrate is evaporated to obtain 3.2g of extract of Pericarp of Akebia quinata(PKake) of brown color.

2) The combined filtrate obtained from 1) is instantly lyophilized to obtain the same amount of extract of Pericarp of Akebia quinata (PKake).

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Example 5

Preparation of extract of Ulmi cortex (PKu)

1) 10g of powder of Ulmi cortex is mixed with 100ml of methanolic water of 50% (V/V) and is extracted for 1hour and filtered. The residue is extracted with the same way and

filtered. The combined filtrate is evaporated to obtain 2.5g of extract of Ulmi cortex (PKu).

2) The combined filtrate obtained from 1) is instantly lyophilized to obtain the same amount of the extract of Ulmi cortex (PKu).

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Prescriptions

General Prescription 1

Prescription composed with 2 kinds of extracts

10 0.3, 0.6, 0.8 and 1.0 weight parts of PKG are respectively added to 1 weight part of PKW and mixed to obtain respective compositions. The compositions are respectively titled to PKWG-0.3, PKWG-0.6, PKWG-0.8 and PKWG-1.0.

General Prescription 2

15 Prescription composed with 2 kinds of extracts

0.1, 0.2, 0.3, 0.4 and 0.5 weight parts of PKgly are respectively added to 1 weight part of PKW and mixed to obtain respective compositions. The respective compositions are respectively titled to PKgly 0.1, PKgly 0.2, PKgly 0.3, PKgly 0.4 and PKgly 0.5.

20 General Prescription 3

Prescription composed with 2 kinds of extracts

0.1, 0.3, 0.5, 0.7 and 0.9 weight parts of PKake are respectively added to 1 weight part of PKW and mixed to obtain respective compositions. The respective compositions are respectively titled to PKake 0.1, PKake 0.3, PKake 0.5, PKake 0.7 and PKake 0.9.

General Prescription 4**Prescription composed with 2 kinds of extracts**

- 5 0.2, 0.5, 0.8, 1.1 and 1.5 weight parts of PKu are respectively added to 1 weight part of PKW and mixed to obtain respective compositions. The respective compositions are respectively titled to PKu 0.2, PKu 0.5, PKu 0.8, PKu 1.1 and PKu 1.5.

Prescriptions composed with 3 kinds of extract

- 10 The following prescriptions are composed with 3 kinds of extracts based upon animal experiments.

General prescription 5**Prescriptions composed with PKW, PKG and PKgly(Prescription PGgly)**

- 15 0.8 weight part of PKG and 0.4 weight part of PKgly are added to 1 weight part of PKW and mixed to obtain prescription PGgly.

General prescription 6**Prescriptions composed with PKW, PKG and PKake(Prescription PGake)**

- 20 0.8 weight part of PKG and 0.5 weight part of PKake are added to 1 weight part of PKW and mixed to obtain prescription PGake.

General prescription 7**Prescriptions composed with PKW, PKG and PKu(Prescription PGu)**

0.8 weight part of PKG and 1.1 weight part of PKu are added to 1 weight part of PKW and mixed to obtain prescription PGu.

In fact, in the case of prescriptions composed of 2 kinds of extracts, all eight parts of
5 PKG, PKgly, PKake and PKu to 1 weight part of PKW can be composed based on the above prescriptions. In the same way, various prescriptions composed of 3 kinds of extracts can be composed based on the above prescriptions. In fact, all weight parts are based on 10g of PKW.

Preparation Examples are illustrated as follows.

10 The above prescriptions are prepared as injections, oral preparations, etc.

Injections: Injections are prepared by dissolving the said prescriptions in physiological sodium chloride solution, Ringer's solution or other nutritive solution and bacterial-filtration or any other bactericidal measures.

Oral preparations: oral preparations are prepared with the said prescriptions by
15 conventional preparation methods.

Preparation examples

Preparation example 1

20 Preparation of PKW 0.8

10g of PKW is dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

Preparation example 2

Preparation of PKWG 0.8

10g of PKW and 8g of PKG are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

5 Preparation example 3**Preparation of PKWgly 0.4**

10g of PKW and 4g of PKgly are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

10 Preparation example 4**Preparation of PKWake 0.5**

10g of PKW and 5g of PKake are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

15 Preparation example 5**Preparation of PKWu 0.8**

10g of PKW and 8g of PKu are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

20 Preparation example 6**Preparation of PGgly**

10g of PKW, 8g of PKG and 4g of PKgly are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

Preparation example 7**Preparation of PGake**

10g of PKW, 8g of PKG and 5g of PKake are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

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Preparation example 8**Preparation of PGu**

10g of PKW, 8g of PKG and 8g of PKu are dissolved in 1liter of physiological sodium chloride solution and bacteria-filtered to prepare solution.

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Preparation example 9

0.5g of PKW and 0.2g of PKgly are mixed with conventional vehicle and pressed to prepare tablet.

15 **Preparation example 10**

0.5g of PKW and 0.3g of PKake are mixed with conventional vehicle and encapsulated to prepare capsule.

Preparation example 11

20 0.5g of PKW and 0.2g of PKu are dissolved in distilled water for injection, filled into ampoule and sterilized to prepare injection.

Preparation example 12

0.5g of PKW, 0.4g of PKG and 0.2g of PKgly are mixed with conventional vehicle and pressed to prepare tablet.

Preparation example 13

5 1g of PKW, 0.2g of PKG and 0.2g of PKake are mixed with conventional vehicle and sealed in envelope coated with polyethylene resin into prepare powder.

The present invention is explained in more detail with experimental examples as follows.

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Analgesic effects for the said prescriptions were firstly screened by using animals. By representatively selecting prescriptions which show superior analgesic effects clinical trials were carried out.

15 Experimental examples

Experimental example with animals

It is regarded that though measuring pains of tumor patients by using animals is impossible, the mechanisms of reducing or eliminating pains for persons and animals are
20 same.

RCI mice were used as animals. After administration of composition of the present invention to the animals, acetic acid is injected into abdominal cavity of the animals. After the administration of the injection into abdominal cavity, the number of times of writhing is recorded. Test results obtained with several representative prescriptions are explained below.

Experimental example 1**1) Measurement of analgesic effect on mouse**

17 groups including 3 mice of body weight of 20-25g per one group are divided and
5 1 group is used as control group. To remaining 16 groups test materials are injected into
abdominal cavities of each mouse following doses and times listed on the Table 1. First from
control group, to each group each 0.2ml of acetic acid of 0.6% is injected into abdominal
cavities. Number of times of writhing of each mouse of each group is measured for 10 min.
Inhibition rates are recorded as percent rate of writhing of groups administered of test
10 materials to those of control group. The results are shown on the Table 1.

As shown from the Table 1, PKW, the extract of Pulsatillae Radix its has powerful
analgesic effect on mouse model. PKWG of the combination of PKW and PKG and PGgly
of the 3 combinations of PKW, PKW and PKgly show inhibition rates of 95% or over.

Table 1 : Inhibition rates of mice on writhing test based on PKW prescriptions

Prescription	dose(ml/kg)	number of writhing	inhibition rate(%)
Control	saline	17.6	0
PKW	0.5	1.33	92.4
	1	0.66	92.2
PKWG0.8	0.5	2.33	86.7
	1.5	0.66	92.2
PKWgly0.4	0.5	6.3	64.2
	1.5	1.33	92.4
PKWake0.5	0.5	10.3	41.4
	1.5	4.6	73.8
PKu0.8	0.5	10.6	39.7
	1.5	7.3	58.5
PGgly	0.5	1	94.3
	1.5	0.33	98.1
PGake	1	11	37.5
	2	5.6	68.1
PGu	1	13.3	24.4
	2	3.6	79.5

Acetaminophene 0.2mg/kg in saline 0.9 ± 0.05

5 2) Analgesic effect with volunteers

By selecting prescriptions having good analgesic effects from the above animal tests, the test materials of the prescriptions are administered to volunteers of cancer patients and evaluated analgesic effects of the test materials. As for the test materials, we selected and used PKW and PGake which are effect from the animal tests. Amounts of the test materials are

0.25ml/kg of PKW and 0.25ml/kg of PGgly. The test materials are administered once/day for 4 days (first injections) and evaluated through asking the degrees of pains to the volunteers. After 14 days from the first injections, the same way of administrations is carried out for 4 days (2nd injections). After 2nd injections, the degrees of pains are evaluated through asking the degrees of pains to the volunteers.

Experimental example 2

Clinical trials with cancer patients

12 patients suffering from various cancers are entered to the trials. The patients whose cancers are already advanced are appealing cancer pains. PKW and PGgly which are effect from the animal tests are selected and injected intravenously. Other analgesics which had been being administered to the patients are stopped. 2 days after of stopping of administration of the other analgesics, 0.25ml/kg of the test materials are injected intravenously once a day for 4 days (first injections) and evaluated through asking the degrees of pains to the patients. After 14 days from the first injections, the same way of administrations is carried out(2nd injections). After the 2nd injections, analgesic effects of the test materials are evaluated through asking the degrees of pains to the patients. The test results are shown on the Table 2.

Table 2 : Evaluations of pains for cancer volunteers**PKW injections**

Volunteers	Before Admin.	After 1st inject.	After 2nd inject.
Kim, O.H. (female, esophageal cancer)	severe	alleviative	no pain
Kim, D.O. (female, liver cancer)	very severe	alleviative	alleviative
Shim, O.C. (female, large int. cancer)	severe	alleviative	no pain
Park, J.S. (male, stomach cancer)	very severe	alleviative	no pain
Park, S.M. (male, parotid cancer)	moderate	no pain	no pain
Whang, J. S. (male, lung cancer)	severe	alleviative	alleviative

5 PGgly injections

Volunteers	Before Admin.	After 1st inject.	After 2nd inject.
Kwon, T.Y. (female, uterine cancer)	severe	alleviative	no pain
Lee, C.H. (female, stomach cancer)	severe	alleviative	alleviative
Chung, K.C. (male, metastasis cancer)	very severe	alleviative	no pain
You J.I. (male, lung cancer)	moderate	no pain	no pain
Kim, O.G. (female, thyroid cancer)	very severe	alleviative	alleviative
Kim, D.C. (male, metastasis cancer)	very severe	no pain	no pain

As shown on the Table 2, all prescriptions of the extract of Pulsatillae Radix and prescriptions based on the extract of Pulsatillae Radix show excellent analgesic effects. These prescriptions have characteristics of having analgesic effect and anti cancer effect simultaneously. For instance, it is regarded that synergistic analgesic effects of the present compositions are achieved, because emphysema by tumor, damage of tissue and the size of tumor are lessened and at the same time analgesic effect are exhibited as pharmacological effects of the composition.

Experimental example 3

10 Acute toxicity

Each 5ml of preparation example 11 are injected intraperitoneally to 10 ICR mice of 25-30g of body weight. No animals are died.

【Industrial Applicability】

15 The most excellence of the present composition shows characteristics of having analgesic effect and anti cancer effect simultaneously. These effects are different from the existing control methods of pain in which anticancer agent and analgesic agent are used separately. In addition, the analgesic effect of the present composition has prolonged duration of effect. As seen from the Table 2, cancer patients do not complain from pain even though 15
20 days have past from the beginning. In the case of the terminal stage of cancer, though administration of the composition of the present invention has stopped, patients (Kim, O.G., Kim, D.C., and Whang, J. S.) did not complain from pains until they died. Therefore, the present composition can be used as analgesic agent in alleviating or treating pain of cancer patient.